

ischaemia and/or stress regulatable agent; and

(iii) a binding agent that binds to a cell surface element of the mononuclear phagocyte wherein the binding agent comprises a viral vector and wherein the binding agent comprises means for ensuring the hypoxia and/or ischaemic and/or stress regulatable agent is internalised into said mononuclear phagocyte.

52. (new) A therapeutic composition according to claim 51 wherein said regulatable agent comprises a therapeutic gene.

53. (new) A therapeutic composition according to claim 52 wherein said gene is under the control of a hypoxia and/or ischaemic and/or stress sensitive agent.

54. (new) A therapeutic composition according to claim 51 wherein said binding agent comprises a ligand adapted to bind to said cell surface element.

55. (new) A therapeutic composition according to claim 51 wherein said means for ensuring the hypoxia and/or ischaemic and/or stress regulatable agent is internalised into said mononuclear phagocyte is further adapted to ensure that a therapeutic gene is incorporated into the nucleus of said mononuclear phagocyte.

56. (new) A therapeutic composition according to claim 51 wherein said viral vector is an adenoviral vector.

57. (new) A therapeutic composition according to claim 51 wherein said viral vector is a lentiviral vector.

58. (new) A therapeutic composition according to claim 51 wherein said

regulatable agent comprises a therapeutic gene encoding a pro-drug activation enzyme.

60. (new) A therapeutic composition according to claim 51 wherein said regulatable agent further, or alternatively, comprises a bioreductively activated pro-drug.

61. (new) A therapeutic composition according to claim 51 wherein said composition further comprises an agent that activates or controls said regulatable agent.

62. (new) A therapeutic composition according to claim 61 wherein said agent controls the expression of a therapeutic gene regulated activating or control product.

63. (new) A therapeutic composition according to claim 51 wherein said therapeutic gene is under the control of an inducible or repressible promoter element.

64. (new) A therapeutic composition according to claim 63 wherein said element comprises a tetracycline repressor DNA sequence.

65. (new) A therapeutic composition according to claim 51 wherein there is further provided a gene encoding a protein that kills mononuclear phagocytes.

66. (new) A therapeutic composition according to claim 51 wherein the mononuclear phagocyte further comprises an agent that is adapted to bind to a mononuclear phagocyte ligand which is typically found on the cell surface of said mononuclear phagocyte.

67. (new) A method for selectively destroying a mononuclear phagocyte comprising:

- (ii) attaching thereto, internalising therein, a cytotoxic, hypoxically and/or ischaemically and/or stress activated agent;
- (iii) transfecting and/or transducing a mononuclear phagocyte with the binding agent; and
- (iv) exposing said mononuclear phagocyte to hypoxic and/or ischaemic and/or stress conditions that occur either artificially by induction or occur/exist naturally; such that the mononuclear phagocyte is selectively destroyed after expression of the cytotoxic, hypoxically and/or ischaemically and/or stress activated agent at the target hypoxic and/or ischaemic and/or stress site.

68. (new) A delivery system for targeting a therapeutic composition to hypoxic and/or ischaemic and/or stress sites wherein the delivery system comprises;

- (i) a hypoxia and/or ischaemic and/or stress regulatable agent; and an agent for controlling the functional effectiveness thereof;
- (ii) a mononuclear phagocyte that has coupled thereto, or internalised therein, the hypoxia and/or ischaemia and/or stress regulatable agent; and
- (iii) a binding agent that binds to a cell surface element of the mononuclear phagocyte wherein said binding agent comprises a viral vector and wherein the binding agent comprises means for ensuring the hypoxia and/or ischaemic and/or stress regulatable agent is internalised into said mononuclear phagocyte.

69. (new) A method for targeting desired hypoxic and/or ischaemic and/or stress

molecule expressed by a mononuclear phagocyte and wherein the binding agent is a viral agent;

- (ii) attaching thereto or internalising at least one of said hypoxic and/or ischaemic and/or stress regulatable agents to the binding agent;
- (iii) exposing said binding agent comprising the hypoxic and/or ischaemic and/or stress regulatable agent to said mononuclear phagocyte; and
- (iv) allowing said mononuclear phagocyte to migrate under conditions that support migration, either on *in vitro* or *in vivo*.

70. (new) A method for treating conditions associated with hypoxic and/or ischaemic and/or stress states comprising administering to an individual to be treated a therapeutic composition according to claim 51.

71. (new) A method for treating conditions associated with hypoxic and/or ischaemic

and/or stress states comprising;

- (i) withdrawing blood and/or serum from an individual to be treated;
- (ii) treating said blood and/or serum *in vitro* with a therapeutic composition according to claim 51; and
- (iii) re-injecting said treated blood and/or serum into the individual either systemically or directly into a hypoxic and/or ischaemic and/or stress area.

72. (new) A therapeutic composition comprising:

1. A therapeutic composition for stress regulatable agent wherein the

(ii) a mononuclear phagocyte that has coupled thereto, or internalised therein, at the hypoxia and/or ischaemia and/or stress regulatable agent; and

(iii) a binding agent that binds to a cell surface element of the mononuclear phagocyte wherein said binding agent comprises a viral vector; wherein the binding agent comprises means for ensuring the hypoxia and/or ischaemic and/or stress regulatable agent is internalised into the mononuclear phagocyte; and wherein said mononuclear phagocyte is capable of delivering the a hypoxia and/or ischaemic and/or stress regulatable therapeutic gene to a hypoxic and/or stress and/or ischaemic tumour site.

73. (new) A therapeutic composition according to claim 72 wherein the therapeutic gene comprises a CyP2B6 gene.--

**REMARKS**

Reconsideration is requested.

Claims 25-50 have been canceled, without prejudice. Claims 51-73 have been added above. Support for the amended claims may be found throughout the specification. No new matter has been added.

Claims have not been added without canceling a corresponding number of claims. Moreover, the claims have been amended to advance prosecution without raising new issues requiring a further search and/or consideration. Entry of the above amendments is requested.